Background: Various doses of ATG have been utilized in RIC allogeneic transplantation targeting T cell depletion, with the goal of decreasing the incidence and severity of both acute and chronic GVHD. This is an update to the previously published data where we showed that lower ATG dose resulted in improved non-relapse mortality and infection rate without compromising control of GVHD.
Methods: We retrospectively analyzed 136 consecutive patients who received RIC HSCT between 2006 and 2010. Following October 2007, ATG dosing was lowered from 7.5 mg/kg (R-ATG) to 6 mg/kg (r-ATG). Progression-free (PFS) and overall survival (OS) were analyzed using the log-rank test. Cumulative incidences of GVHD were analyzed using Gray's test, accounting for competing risks.
Results: Thirty-nine patients received R-ATG and 97 received r-ATG. There were no significant differences in age, gender, KPS, degree of HLA match, prior autografts, donor/recipient CMV status, and CD34 cell dose between the two groups ($P >$ .15). More patients were transplanted with r-ATG than R-ATG for CLL and fewer with AML/MDS/NHL/HD/other histologies ($P = .02$). Time to platelet engraftment as well as donor-cell chimerism at days +30, +90, +180 were not significantly different between the groups, but time to neutrophil engraftment was shorter with R-ATG ($P = .001$). Proportions of aGVHD II-IV were 52% and 41% ($P = .34$) in r-ATG and R-ATG respectively and proportions of cGVHD were 40% and 53% ($P = .23$). Further, no significant differences in the cumulative incidence of GVHD were observed (Figure 1). The R-ATG group experienced more episodes of bacterial infections than the r-ATG cohort (54% vs. 8%; $P < .0001$). No differences in PFS ($P = .69$) or OS ($P = .95$) were observed between the cohorts.
Conclusion: r-ATG did not result in an increase incidence of acute or chronic GVHD. No PFS or OS differences were observed between the cohorts; however, R-ATG resulted in a higher proportion of bacterial infections.

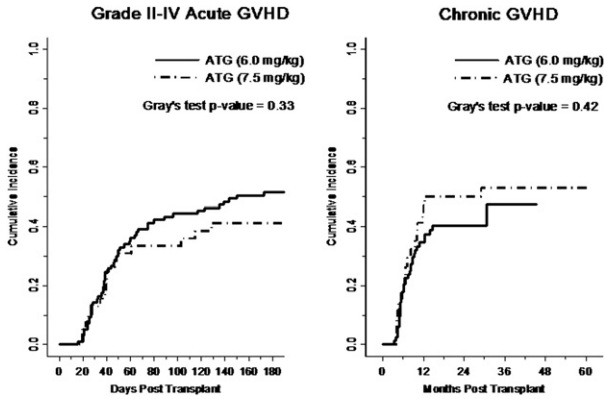

Figure 1. Acute and chronic GVHD

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Soluble Aminopeptidase N (CD13) Is a Diagnostic Biomarker of Late-Onset Chronic Graft Vs. Host Disease in Adults

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Background: Chronic graft vs. host disease (cGVHD) is a major cause of morbidity and mortality after allogeneic HSCT. As an insidious onset and heterogeneous presentation renders this disease difficult to diagnose, there is a need for validated diagnostic biomarkers. Previously, soluble aminopeptidase N (CD13) was identified in a pediatric study as a biomarker for early onset cGVHD (diagnosed 3-9 months post transplant). Aminopeptidase N is a protease involved in immunoregulation on several levels; functions include attraction of T cells, antigen presentation, facilitation of adhesion and phagocytosis. Although it is integrated in the membrane of several cell types it can also be cleaved into soluble aminopeptidase N. In this study, we tested the potential plasma biomarker soluble aminopeptidase N in an adult population of late onset cGVHD patients using both a targeted method (enzymatic assay) as well as a non-targeted approach (proteomics).
Methods: Samples used in this study were frozen, EDTA-treated plasma samples derived from a single institution participating in the Chronic GVHD Consortium and consisted of 17 cases and 21 time-matched controls, all from adult patients. Cases were within 1 month of diagnosis of late-onset cGVHD (onset >9 months post transplant). Time posttransplant for cases vs. controls was 12 (9.2-26.8) vs. 11.9 (5.3-13.5) months, respectively. Other potential clinical variables included age at sample collection, gender, graft source, donor type, conditioning intensity, prior acute grade II-IV GVHD, and months from sample collection. Aminopeptidase N activity was determined by cleavage of L-leucine-p-nitroaniline; quantitative proteomic analyses were done with iTRAQ.
Results and Conclusions: Plasma from cGVHD patients had significantly higher mean levels of aminopeptidase N enzyme activity than did plasma from control patients (0.30 vs. 0.18 mU/ml, respectively $P = .0008$). Proteomic analyses using the same samples revealed that this difference was not restricted to activity; aminopeptidase N showed the most significant difference in protein levels corresponding to presence or absence of cGVHD of all the proteins identified. Relative amounts of soluble aminopeptidase N were 1.44 vs. 0.9, in cases and controls, respectively ($P = .0042$). This study supports soluble aminopeptidase N as a potential diagnostic biomarker in adult GVHD. These results will be validated in a larger population which also includes early onset cGVHD.

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Long-Term Survival After Allogeneic Haematopoietic Cell Transplantation for Acute Myeloid Leukemia. Comparable Results From Myeloablative and Non-Myeloablative Conditioning in Young and Elderly Patients

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Nonmyeloablative (NM) conditioning in allogeneic transplantation is increasingly used in patients aged over 50 years with acute myeloid leukemia (AML). In this single-center retrospective study, we report the results of NM and myeloablative (MA) conditioning in 207 consecutive AML